PATENT APPLICATION

I hereby certify that this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

2-24-04
Date

Kim M Goplen
Kim Goplen

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Cindy A. Sprecher, Scott R. Presnell, Zeren Gao, Theodore E. Whitmore, Joseph L. Kuijper, Mark F. Maurer
Serial No.	:	09/892,949
Filed	:	June 26, 2001
For	:	NUCLEIC ACID ENCODING CYTOKINE RECEPTOR ZCYTOR17 (As Amended)
Examiner	:	Hamud, F.
Art Unit	:	1647
Docket No.	:	00-42
Date	:	February 24, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §132

Sir:

I, Janine Bilsborough, declare and say as follows:

1. I received a B.S in Biology from the University of Queensland, Brisbane, Australia in 1990, an Honors Degree in Microbiology in 1991, and Ph.D. in Public Health from the University of Queeensland, Brisbane, Australia in 1996. I had a postdoctoral fellowship at the Ludwig Institute for Cancer Research in Brussels, Belgium from August 1996 to June 2000. My second postdoctoral fellowship was at Immunex Corporation, Seattle, Washington from August 2000 to December 2002. Since January 2003 I have been a scientist at Zymogenetics, Seattle, Washington.

2. My research activities include, but are not limited to, the study of cytokine receptor genes and the identification and characterization of their receptors. I have several publications and have been invited to speak at numerous symposia on these and other related topics.

3. I have read and am familiar with the Office Action mailed August 26, 2003, with respect to the above-identified application, and make this Declaration in support of the patentability of the claims of patent application Serial No. 09/892,949.

4. The specification of patent application Serial No. 09/892,949 provides, for example, at page 55, lines 7-19, and at page 62, line 6, that zcytor17 plays a role in inducing inflammation by immune response cells, e.g., monocytes and T cells, upon binding zcytor17 ligand.

5. Monocytes patrol the bloodstream searching for foreign antigens. Monocytes engulf, digest, and subsequently present small portions (peptides) of the foreign antigen on their surface in conjunction with MHC class II.

6. CD4+ T cells recognize antigens that are presented in association with MHC class II molecules as described in paragraph 5. Once recognized, CD4+ T cells produce numerous cytokines, e.g., human interferon-gamma ("hIFNγ"), to enhance inflammation and antiviral responses.

7. CD8+ T cells are activated by cytokines released by the activated CD4+ T cells of paragraph 6. Activated CD8+ T cells recognize cells presenting foreign peptides in association with MHC class I on their surface. Once recognized, CD8+ T cells destroy the cells compromised by infection or mutation.

8. Annotation of the cell types and growth conditions that affect zcytor17 expression is a useful means of elucidating its function and predicting a source of ligand. Accordingly, cDNA libraries from a wide variety of tissues and cell types were surveyed by polymerase chain reaction ("PCR") using oligonucleotide primers specific for

zcytor17. Of the strong positive PCR signals two were from the human monocyte cell lines U937 and THP1. Human monocyte cell lines U937 and THP1 were further analyzed by Northern Blot. A prominent mRNA band was seen in U937, while a fainter band was seen in THP1. Example 3; page 105, line 4 to page 107, line 17 of the instant application. Thus, zcytor17 is expressed in monocytes.

9. THP1 cells were grown in various media to stimulate cellular proliferation, including stimulants such as hIFNγ. THP1 cells treated with hIFNγ for 30-hours had a twenty-fold increase in zcytor17 mRNA expression over nontreated THP1 cells. Example 3, page 108, lines 1-22 of the instant application. Thus, I submit that hIFNγ, a well-known proinflammatory cytokine, is a potent stimulator of zcytor17 mRNA expression in monocytes. Accordingly, zcytor17 expression in monocytes is upregulated during an inflammatory response.

10. Zcytor17 mRNA levels in CD4+ and CD8+ T cells were determined by real-time quantitative reverse transcriptase polymerase chain reaction ("RT-PCR") assay. mRNA levels of zcytor17 in resting CD4+ and CD8+ T cells were below detection. In contrast, however, zcytor17 mRNA levels in activated CD4+ and CD8+ T cells (incubated 4-hours with anti-CD3 and anti-CD28 antibodies, respectively) were substantially upregulated. Thus, zcytor17 expression in CD4+ and CD8+ T cells is upregulated in an immune-mediated inflammatory response.

11. Expression of full-length human zcytor17 (specifically, SEQ ID NO:2 of the above-identified patent application) and human Oncostatin M receptor-beta (OSMR) in BaF3 cells, an immortalized murine bone marrow-derived pro-B-cell line the growth and proliferation of which depends on the presence of mIL-3, provided a proliferative assay for zcytor17 ligand identification as similarily described on page 51, line 3 through page 52, line 8 of the instant application. Briefly, expression vectors encoding full-length zcytor17 and OSMR were transfected into BaF3 cells. The cells were spun down and washed three times to ensure the removal of mIL-3. In the absence of mIL-3, upon which BaF3 cells growth and survival depend, BaF3 cells undergo death by apoptosis.

Proliferation of the BaF3/zcytor17/OSMR cells was assessed using conditioned media from activated human peripheral blood cells selected for CD3 (cell surface marker unique to cells of lymphoid origin, particularly T cells). See Examples 1-5 of U.S. Patent Application Serial No. 10/351,157, filed January 21, 2003, a copy of which was mailed to the Examiner on May 22, 2003 and whose consideration was noted in paragraph 4b of the Office Action dated August 26, 2003.

12. Results of the assay confirmed the proliferative response of the BaF3/zcytor17/OSMR cells to a factor present in the activated CD3+ selected human cell conditioned media. Screening of a primary human activated CD3+ selected cDNA library revealed the proliferative factor to be a novel four-helix bundle cytokine, zcytor17 ligand. See Example 5 of U.S. Patent Application Serial No. 10/351,157, filed January 21, 2003.

13. The untransfected cells in the assay did not proliferate in response to zcytor17lig. Moreover, a soluble zcytor17 receptor diminished the proliferative activity of zcytor17lig in BaF3/zcytor17/OSMR cells. See Example 5 of U.S. Patent Application Serial No. 10/351,157, filed January 21, 2003.

14. Further evidence that zcytor17 plays a physiological role in inducing inflammation by proliferating immune response cells, in situ hybridization was performed on involved and uninvolved tissue samples of human patients diagnosed with inflammatory bowel disease ("IBD") and psoriasis. In both cases, zcytor17 RNA expression was significantly upregulated in the diseased tissue samples. Thus, zcytor17 is upregulated in affected IBD and psoriatic tissue.

15. As a result of the experimental evidence (paragraphs 8-14) and reasoning discussed above (paragraphs 4-7), I submit that the zcytor17 polypeptides of U.S. Application Serial No. 09/892,949 are able to induce inflammation by proliferating immune response cells. Thus, I submit that zcytor17 exhibits a physiologically significant, real-world use.

16. I further declare that statements made herein of my knowledge are true, and that all statements made on information are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 20th February, 2004 By: